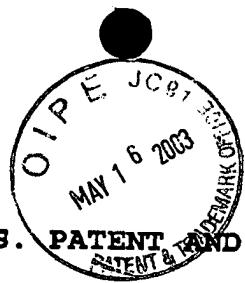


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Inventor **Tibor GIZUR et al**
Patent App. **09/856,517 (US Nat'l phase of PCT/HU99/00102)**
Filed **21 May 2001** Conf. No. **9138**
For **PROCESS FOR THE SYNTHESIS OF 1-(AMINOMETHYL)CYCLOHEXYL-ACETIC ACID**
Art Unit **1625** Examiner **Oh, T**
Hon. Commissioner of Patents
Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR 1.132

I, **Tibor GIZUR**, a citizen of Hungary, residing at
Avarszallas u., 30, H-1162, Budapest, Hungary, a citizen of Hungary, declare as follows:

THAT I was awarded in 1995 the degree of PhD in chemical engineering from the Technical University of Budapest;

THAT I have a number of years of experience in the synthesis of organic compounds;

THAT my curriculum vitae may be attached to this declaration;

THAT I am an applicant in U.S. Patent Application Serial No. **09/856,517** filed 21 May 2001 and directed to A PROCESS FOR THE SYNTHESIS OF 1-(AMINOMETHYL)CYCLOHEXYL-ACETIC ACID;

THAT I have been informed that the Examiner in said U.S. patent application has questioned whether any other hydrogenation catalyst besides palladium-on-charcoal can effectively catalyze the

hydrogenation of the nitro compound of the Formula (II) to yield the 1-(aminomethyl)-cyclohexyl-acetic acid of the Formula (I);

THAT in order to establish that a variety of hydrogenation catalysts well known to those "skilled in the art" may be used to effectively catalyze the hydrogenation of the compound of the Formula (II) to yield the desired compound of the Formula (I), I have either personally conducted or supervised the carrying out of the following tests:

TESTS

We have carried out additional Examples 3 and 4 showing catalytic hydrogenation of the compound of the Formula (II) where R is hydrogen to yield 1-(aminomethyl)cyclohexyl acetic acid of the Formula (I). Instead of palladium, the catalysts tested were Raney nickel and Adams catalyst. The examples are as follows:

Example 3

1-(nitromethyl)cyclohexane acetic acid (6.27 g; 0.031 mol) was dissolved in methanol (75 ml). To the solution Raney Ni catalyst (1 g) was added and was hydrogenated at atmospheric pressure. The catalyst was filtered off and the filtrate was evaporated in vacuo. To a residue was added tetrahydrofuran (60 ml). The crystalline product was filtered off and dried.

Yield: 2.1 g (39.6 %)

Melting point: 165-9°C

Example 4

1-(nitromethyl)cyclohexane acetic acid (6.27 g, 0.031 mol) was dissolved in methanol (75 ml). To a solution Adam's catalyst (0.07 g) was added and was hydrogenated at atmospheric pressure. The catalyst was filtered off and the filtrate was evaporated in vacuo. To the residue was added tetrahydrofuran (60 ml). The crystalline product was filtered off and dried.

The Examiner has made an argument that catalysis is an unpredictable art and more than routine experimentation would be needed to determine which hydrogenation catalysts known in the art would actually work to reduce the present Formula (II) compound to form the Formula (I) compound and which would not work.

THAT I conclude that these examples show clearly that the hydrogenation process can be carried out with other types of hydrogenation catalysts besides palladium-on-charcoal. I further conclude that catalytic hydrogenation of a nitro compound of the Formula (II) is not so unpredictable as the Examiner believes. Catalytic hydrogenation of nitro compounds to obtain amino compounds has been known to those "skilled in the art" for many years and such a hydrogenation step is a common process used in organic synthesis. In such a process several types of hydrogenation catalysts can be used interchangeably so that one hydrogenation catalyst can be routinely substituted for another to obtain the same product with perhaps only some difference in product yield or purity. Therefore in principle it is highly predictable that the well-known and commonly used catalysts may be substituted for

one another in hydrogenation of a nitro compound to form the corresponding amino compound. For instance one "skilled in the art" knowing that the use of Raney nickel to catalyze the hydrogenation of a nitro compound to form the amino compound would also work if palladium were substituted as hydrogenation catalyst for the Raney nickel.

THAT I am aware of no information inconsistent with that presented above or which would lead one to a contrary conclusion; and

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further

THAT these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 07.01. 2003.

Signed: Tibor GIZUR

Tibor GIZUR



Name : Tibor GIZUR

Date of birth: 13/05/1954

Education

- 1979 chemical engineer (Technical University of Budapest)
- 1983 university doctor's degree (Technical University of Budapest)
- 1984 candidate in chemical sciences (Hungarian Academy of Sciences)
- 1995 Ph.D. (Technical University of Budapest)

Scientific work

32 publications in scientific periodicals

Inventor in 34 patents